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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/554,314	04/19/2006	Christoph Hock	37998-237479	2670

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EXAMINER	
WANG, CHANG YU	

ART UNIT	PAPER NUMBER
1649	

MAIL DATE	DELIVERY MODE
08/17/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/554,314	HOCK ET AL.	
	Examiner	Art Unit	
	Chang-Yu Wang	1649	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 June 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-18* is/are pending in the application.

4a) Of the above claim(s) *11-17* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-10 and 18* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-18* are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *12/24/05* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of Application/Election/Restrictions

1. Applicant's election without traverse of Group I (claims 1-10) in the reply filed on June 1, 2007 is acknowledged.

2. Claims 1-17 and newly added claim 18 are pending. Claims 11-17 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to nonelected inventions, there being no allowable generic or linking claim. Election was treated as made **without** traverse in the reply filed on June 1, 2007. Claims 1-10 and newly added claim 18 are under examination in this office action.

Information Disclosure Statement

3. The listing of references in the specification is not a proper information disclosure statement. 37 CFR 1.98(b) requires a list of all patents, publications, or other information submitted for consideration by the Office, and MPEP § 609.04(a) states, "the list may not be incorporated into the specification but must be submitted in a separate paper." Therefore, unless the references have been cited by the examiner on form PTO-892, they have not been considered.

Specification

4. The title is objected to because the title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed.

5. The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code (see p.13). Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01.

6. The following guidelines illustrate the preferred layout for the specification of a utility application. These guidelines are suggested for the applicant's use.

Arrangement of the Specification

As provided in 37 CFR 1.77(b), the specification of a utility application should include the following sections in order. Each of the lettered items should appear in upper case, without underlining or bold type, as a section heading. If no text follows the section heading, the phrase "Not Applicable" should follow the section heading:

(a) TITLE OF THE INVENTION.
(b) CROSS-REFERENCE TO RELATED APPLICATIONS.
(c) STATEMENT REGARDING FEDERALLY SPONSORED RESEARCH OR DEVELOPMENT.
(d) THE NAMES OF THE PARTIES TO A JOINT RESEARCH AGREEMENT.
(e) INCORPORATION-BY-REFERENCE OF MATERIAL SUBMITTED ON A COMPACT DISC.
(f) BACKGROUND OF THE INVENTION.
    (1) Field of the Invention.
    (2) Description of Related Art including information disclosed under 37 CFR 1.97 and 1.98.
(g) BRIEF SUMMARY OF THE INVENTION.
(h) BRIEF DESCRIPTION OF THE SEVERAL VIEWS OF THE DRAWING(S).
(i) DETAILED DESCRIPTION OF THE INVENTION.
(j) CLAIM OR CLAIMS (commencing on a separate sheet).
(k) ABSTRACT OF THE DISCLOSURE (commencing on a separate sheet).
(l) SEQUENCE LISTING (See MPEP § 2424 and 37 CFR 1.821-1.825. A "Sequence Listing" is required on paper if the application discloses a nucleotide or amino acid sequence as defined in 37 CFR 1.821(a) and if the required "Sequence Listing" is not submitted as an electronic document on compact disc).

Claim Rejections - 35 USC § 112

7. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-10 and 18 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for detecting an increased level of immunostaining on brain sections of $APP^{SW}xPS1^{M146L}$ double-transgenic mice or increased levels of antibodies against β-amyloid in serum and CSF samples of Alzheimer disease (AD) patients who are immunized with Aβ peptides, AN1792(QS-21), and detecting a positive correlation between the increased immunostaining and improvement of immunization treatment in AD patients, does not reasonably provide enablement for a method of monitoring an immunotherapy in a subject suffering from an amyloidogenic disease or a neurodegenerative disease associated with abnormal protein aggregates by contacting all types of test samples with all forms of amyloid plaque or abnormal protein aggregates-containing samples and comparing the level of immunoreactivity to an unknown reference value that represents a undefined disease or undefined health status as broadly claimed. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims.

"There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is 'undue'. These

factors include, but are not limited to: (A) The breadth of the claims; (B) The nature of the invention; (C) The state of the prior art; (D) The level of one of ordinary skill; (E) The level of predictability in the art; (F) The amount of direction provided by the inventor; (G) The existence of working examples; and (H) The quantity of experimentation needed to make or use the invention based on the content of the disclosure.
In re Wands, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)". See MPEP § 2164.01.

Claims 1-7 and 18 are directed to a method of monitoring an immunotherapy in a subject suffering from an amyloidogenic disease comprising contacting a test sample with an amyloid plaque-containing sample, determining immunoreactivity of the test sample of a subject to a reference value that represents a known disease or health status or a status prior to onset of immunotherapy. Claims 8-10 are directed to a method of monitoring an immunotherapy in a subject suffering from an neurodegenerative disease associated with the deposition of abnormal protein aggregates comprising contacting a test sample with abnormal protein aggregates - containing sample, determining immunoreactivity of the test sample of a subject to a reference value that represents a known disease or health status or a status prior to onset of immunotherapy. Applicants describe a method of detecting anti-Aβ peptides antibodies from AD patients immunized with Aβ1-42, AN1792(QS-21) using the tissue amyloid plaque immunoreactivity (TAPIR) assay, which is an immunohistochemical staining on brain sections of $APP^{SW}xPS1^{M146L}$ double-transgenic mice. Applicants show that 20 out of 30 patients with generation of anti-Aβ antibodies that can be detected by

an increased immunolabeling on $APP^{SW}xPS1^{M146L}$ brain sections have significantly slower rates of decline in cognitive functions and daily activities as compared to patients without such antibodies. The clinical improvement is determined by the Mini Mental State Examination, the Disability Assessment for Dementia and the visual paired delayed recall test from the Wechsler Memory Scale. Further, the specification teaches "the analyses of antibody titers measured by ELISA failed to predict the clinical outcome" (p.2) and also teaches "the TAPIR scores of the immune sera as determined by analyzing human β-amyloid on brain sections of transgenic mice were more predictive for the therapeutic outcome than antibody titers measured by ELISA" (p.7).

Based on the prior art and the specification, Applicant is enabled for monitoring an immunotherapy in patients suffering from AD by obtaining test samples from patients immunized with Aβ1-42 and detecting generation of anti-Aβ antibodies; in particular generation of antibodies that can be detected by an increased immunostaining on brain sections containing human amyloid-plaque or using brain sections of $APP^{SW}xPS1^{M146L}$when compared to controls without generation such antibodies. However, the claims as written are not limited to the method as set forth above. Applicant is not enabled for a method of monitoring an immunotherapy without knowing a reference value of a control, a specific disease or a defined health status as recited in the claims. Although the specification describes several examples of diseases on p. 3, the specification fails to provide sufficient guidance as to what specific disease, health status or reference value might be and how they would correlate with immunotherapy.

Thus, a skilled artisan would not know how to use the claimed method commensurate in scope with the specification without undue experimentation.

In addition, claims 1 and 5 recite "immunized with an amyloid component" and "an amyloid-plaque-containing sample". Claims 8 and 9 recite "immunized with abnormal protein aggregates" and "an abnormal protein aggregate-containing sample". It is known in the art that immunoreaction between an antigen and an antibody requires the antibody to specifically recognize the epitope on the specific antigen, wherein the epitope of the antigen is the same as in the immunogen for the antibody (Paul, Fundamental Immunology, (textbook), 1993, pp. 292-295, under the heading "Fv Structure and Diversity in Three Dimensions"). However, Applicants fail to recite a specific antigen or epitope for an amyloid component and an amyloid-plaque-containing sample as in claims 1 and 5, and also for abnormal protein aggregates and an abnormal aggregate-containing sample as in claims 8 and 9. There is no correlation between the recitations of the structurally undefined immunogens and structurally undefined immunogen-containing samples (an amyloid-plaque-containing sample in claims 1 and 5, and abnormal protein aggregates and an abnormal aggregate-containing sample in claims 8 and 9). Thus, it is unpredictable whether all forms of immunogens (an amyloid component or abnormal protein aggregates) as recited in claims 1 and 8 would immunoreact with all forms of antigen-containing samples for determining the level of immunoreactivity that is also not defined (i.e. cellular immunoreactivity of T cells or B cells or humoral immunoreactivity). For example, immunizing a subject with an amyloid component such as tau protein will not generate an antibody against APP or a fragment,

or derivative or a mutant thereof as recited in claim 7 because immunization with tau will result in generation of anti-tau antibodies, which will not immunoreact with APP or its derivatives. In addition, immunizing a subject with an abnormal protein aggregate in Huntington disease such as poly-Q as relating to claim 8 will not generate an antibody against protein aggregates such as amyloid in AD because immunization with polyQ will result in generation of anti-polyQ, which will not immunoreact with amyloid in AD. Thus, Applicants are not enabled for a method of monitoring an immunotherapy by immunizing with a structurally undefined immunogen (an amyloid component or abnormal protein aggregates) and also detecting its immunoreactivity with a sample containing a structurally undefined immunogen. Since Applicants fail to limit a specific and defined disease and a specific corresponding abnormal protein and abnormal protein aggregate-containing sample, a skilled artisan would not know how to use the invention as currently claimed.

Therefore, in view of the necessity of experimentation, the limited working examples, the unpredictability of the art, and the lack of sufficient guidance in the specification, one of skill in the art would be required to perform undue experimentation to practice the claimed invention as it pertains to a method of monitoring an immunotherapy in a subject suffering from an amyloidogenic disease or an neurodegenerative disease associated with the deposition of abnormal protein aggregates.

8. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-10 and 18 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1-10 and 18 are indefinite because Applicants recite "a reference value representing a known disease or health status, or representing the status of prior to onset of said immunotherapy" in claims 1 and 8. The rest of claims are indefinite as depending from indefinite claims 1 and 8. Although Applicants describe several diseases on p . 3 of the specification, the description is not definite because there is no specific description what would be considered or not considered as a reference value, a known disease, health status, and the status of prior to onset of said immunotherapy, and would be within the scope of the claims. The disclosure fails to set forth the metes and bounds of what is encompassed within the definitions of such a reference value, a known disease, health status, and the status of prior to onset of said immunotherapy; and thus the claims are indefinite.

Claim Rejections - 35 USC § 102

9. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1-4, 8 and 18 are rejected under 35 U.S.C. 102 (b) as being anticipated by Dodel et al. (EP1172378, published on Jan 16, 2002 as cited in the previous office action).

Dodel et al. (EP1172378) (Dodel (EP'378)) teach a method of monitoring an immunotherapy in a subject suffering from AD (i.e. an amyloidogenic disease or a neurodegenerative disease associated with an abnormal protein aggregate as in claims 1-4, 8 and 18; see col. 6, [0036]-col.7, [0041]). Dodel (EP'378) teaches AD patients administered with an anti-Aβ antibody (i.e. samples from a subject suffering from an amyloidogenic disease and immunized against Aβ) and also teaches detection of the levels of anti-Aβ antibodies and Aβ peptides (i.e. an amyloid plaque or abnormal protein aggregate-containing sample as in claims 1 and 8) in plasma and CSF (as in claims 4 and 18) as compared to controls or before treatment (i.e. comparing the level of immunoreactivity between a test sample and an amyloid plaque-containing sample and reference value as in claims 1-4, 8 and 18; see col.3 [0019]; col. 6 [0038]). Dodel (EP'378) teaches that AD patients treated with anti-Aβ antibodies show reduced Aβ burden in the brain of AD patients, which is an inherent result of an increased level of immunoreactivity and a positive outcome (as in claims 4 and 8; see col.7 [0041]). Thus, claims 1-4, 8 and 18 are anticipated by Dodel et al. (EP1172378).

10. Claims 1-10 and 18 are rejected under 35 U.S.C. 102 (e) as being anticipated by Schenk et al. (US Patent No. 6787523, published Sept 7, 2004, priority Dec 2, 1997).

Schenk (US'523) teaches a method of monitoring an immunotherapy in a subject suffering from an amyloidogenic disease or a neurodegenerative disease associated with an abnormal protein aggregate (as in claims 1-2 and 8; see col. 4, lines 27-38; cols. 17-19; cols 22-28). Schenk (US'523) teaches immunizing patients with AD or a transgenic animal model of AD, PDAPP, with Aβ peptides including AN1792 (i.e. AD is an amyloidogenic disease and is also a neurodegenerative disease associated with an abnormal protein aggregate as in claims 1 and 8; AN1792 is β-amyloid and an amyloid component as in claims 1 and 3; see col.22, line 60-col.28). Schenk (US'523) also teaches a method of detecting the level of antibodies in serum and CSF (as in claims 4 and 18; see col.19, lines 3-4) after immunization with AN1792 by ELISA and also by an immunohistochemical method using brain sections of PDAPP transgenic mice or AD patient brain sections as compared to controls (i.e. a brain section of transgenic PDAPP mice is an amyloid plaque-containing sample as in claims 1, abnormal protein-containing sample as in claim 9, and a sample of a transgenic nonhuman animal as in claims 5-7, 9,10; see col.19, lines 6-32; cols.22-28). Schenk (US'523) teaches detection of an increased level of immunoreactivity on brain sections by contacting the sections with serum or the CSF containing anti-Aβ antibodies from animals that show increased clearance of Aβ burden, which is an indicative of improvement of clinical outcomes (as

in claims 1 and 8; see cols.22-28). Thus, claims 1-10 and 18 are anticipated by Schenk et al. (US Patent No. 6787523).

Claim Rejections - 35 USC § 103

11. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1-10 and 18 are rejected under 35 U.S.C. 103(a) as being unpatentable over Dodel et al. (EP1172378, published on Jan 16, 2002 as cited in the previous office action) in view of Schenk et al. (Nature. 1999. 400: 173-177).

Dodel et al. (EP1172378) teach as set forth at paragraph 8 but fails to teach that an amyloid plaque-containing sample and an abnormal protein aggregate-containing sample are derived from transgenic animals or their tissues as in claims 5-7 and 9-10.

Schenk et al. teach immunization of PDAPP transgenic mice with Aβ peptides, AN1792, and detecting the levels of anti-Aβ antibodies by ELISA and immunostaining

on brain sections of PDAPP transgenic mice (i.e. as in claims 5-7 and 9-10; see p. 174-175). Schenk et al. teach an increased immunoreactivity in brain sections of animals that are immunized with Aβ because these sections show clearance of Aβ burden (i.e. as in claims 6-7 and 10; see p.175). The teachings of Schenk et al. provide a motivation and expectation of success in detecting an increased immunoreactivity in samples containing amyloid-plaque (i.e. abnormal protein aggregates) in brain tissue of transgenic animals (as in claims 5-7 and 9-10) that have the same epitopes as Aβ (immunogen).

It would have been obvious to one of ordinary skill in the art at the time the instant invention was made to use brain sections of transgenic animals containing amyloid plaques (abnormal protein aggregates) as a tool to detect the antibody level of immunization and the immunoreactivity of immunogens and antibodies against the immunogens. The person of ordinary skill in the art would have been motivated to do so because animals immunized with Aβ generate anti-Aβ antibodies against Aβ plaques and show reduced Aβ burden or increased Aβ clearance, which is an increased level of immunoreactivity of antibodies against Aβ, as taught by Schenk et al.. Thus, one of ordinary skill in the art would have expected success in monitoring an immunotherapy in a subject suffering from AD by obtaining test samples from patients immunized with Aβ, detecting an increased level of immunoreactivity between an antigen and an antibody on brain sections of transgenic animals that have the same epitopes as immunogens of immunization, and using the increased immunoreactivity as an indicator of improvement of the immunotherapy in AD.

Conclusion

NO CLAIM IS ALLOWED.

Any inquiry of a general nature or relating to the status of this general application should be directed to the Group receptionist whose telephone number is (571) 272-1600.

Papers relating to this application may be submitted to Technology Center 1600, Group 1649 by facsimile transmission. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). Should applicant wish to FAX a response, the current FAX number for Group 1600 is (571) 273-8300.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Chang-Yu Wang whose telephone number is (571) 272-4521. The examiner can normally be reached on Monday-Thursday and every other Friday from 8:30 AM to 5:30 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan, can be reached at (571) 272-0841.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/CYW/
Chang-Yu Wang, Ph.D.
August 8, 2007

CHRISTINE J. SAOUD
PRIMARY EXAMINER
Christine J. Saoud

INTERNATIONAL SEARCH REPORT

International Application No
PCT/EP 03/11413

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 G01N33/68

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 G01N

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)
EPO-Internal, BIOSIS

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 5 164 295 A (KISILEVSKY ROBERT ET AL) 17 November 1992 (1992-11-17) abstract; claims 1,4 ---	11-15
X	DU Y ET AL: "Reduced levels of amyloid beta-peptide antibody in Alzheimer disease" NEUROLOGY, vol. 57, no. 5, 11 September 2001 (2001-09-11), pages 801-805, XP009026218 ISSN: 0028-3878 abstract page 804, right-hand column, paragraphs 2,3; table 1 --- -/--	1-10

[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

° Special categories of cited documents:

'A' document defining the general state of the art which is not considered to be of particular relevance

'E' earlier document but published on or after the international filing date

'L' document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

'O' document referring to an oral disclosure, use, exhibition or other means

'P' document published prior to the international filing date but later than the priority date claimed

'T' later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

'X' document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

'Y' document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

'&' document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
24 February 2004	12/03/2004

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL – 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Weijland, A

Form PCT/ISA/210 (second sheet) (July 1992)